PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	A five year study of cardiac arrest management in general practice in Ireland
AUTHORS	Bury, Gerard; Headon, Mary; Egan, Mairead; Dowling, John

VERSION 1 - REVIEW

REVIEWER	Dr. Richard Verbeek Assistant Professor, University of Toronto Toronto, Ontario, Canada I have no competing interests.
REVIEW RETURNED	20-Jan-2013

THE STUDY	The research question should be better defined. The study is described as reporting the "impact" of GP use of an AED and advanced life support. Firstly,the only intervention that GPs appear to have provided is the use of an AED. No data on any advanced life has been provided. Secondly, it is unclear if the goal was to measure a) willingness of GPs to respond,b) feasibility of implementing a GP program, c) effect on the GP program in improving a predetermined outcome etc. This appears to be largely a program feasibility study in urban, rural and mixed settings. This should be made clear. It is not clear how sites were selected for participation. Were all 2,000 general practices in Ireland invited initally? Were specific pratices targeted to be invited and if so how were they identified? How many invited practices declined to participate and were these in any way different from those who accepted to participate? It would be useful to more fully describe the practices described as urban, rural, mixed. Perhaps census data about population densities etc is available. It would be useful to know something about the training. It may have been reported in the 2009 initial MERIT Project report however it should be summarised here. Was there any follow up training or support for partcipating practices? There is no description as to how the GP "response system" actually functioned. How did a GP even become aware of a cardiac arrest? By what means did a GP respond? The main outcome measure is not explictity stated. If the main

	outcome relates to feasibility then one would want to know how many opportunites there were for GPs to respond and how many opportunities were actually acted on. This data is not reported. It may be that GPs only responsed to a very low proportion of OHCA that they actually were aware of. There may also be substantial differences between urban vs rural vs mixed settings. The conclusions and key messages seem to overstate the main findings. They imply that a GP response to an OHCA results in successful outcomes and higher survival rates. The available data do not support this notion. The conclusions and key messages should focus on the feasibility of implementing this kind of program but should not imply it results in improved outcomes. As an observational study to describe the experience of GPs that statisitics are fine. However there is no specific description in the methods regarding calculation of ORs. The ORs are not reported as to whether they are adjusted or unadjusted ORs, although they are likley unadjusted. Clinically it would be important to report an adjusted OR for "GP delivered first AED in relation to hospital discharge" especially if one is attempting to determine whether the GP response is independantly associated with an improved outcome.
RESULTS & CONCLUSIONS	The results support the feasibility of training GPs with the outcome that they respond to OHCA at least some of the time. I think additional information regarding this outcome would be enlightening as previously described. The results do not support the idea that this program leads to increased survival of OHCA. I have previously addressed several issues related to interpretation and conclusions. I do not think the data supports the statement in the conclusion that "all GPs in rural practice should be equipped with defibrillators". The data may support it is feasible to do this and that there is a potential for improved outcomes however further light needs to be shed on whether outcomes will actually be improved which to me is a requirement to conclude that all GPs should be equipped. This would ideally be answered by a controlled trial, however given the complexity invovled, a high quality observational study using reqression analysis to determine whether a GP response with an AED to an OHCA is independantly associated with increased survival may be more reasonsable to consider. As a result the message behind this report is not as clear it could be. Focussing on the feasibility of the MERIT program would go a long way to improving the clarity of the message.
REPORTING & ETHICS	There is no consort diagram. This could be comprised of how many GP practices there are in Ireland, how many were invited, how many participated, how many OHCAs there were, how many were responded to by a GP.
GENERAL COMMENTS	I find this to be a very intriguing study which describes a highly innovative and potentially promising approach to community

	response to OHCA. I think this paper would be improved by focussing more clearly on the stucture and feasibility of the MERIT program and limiting comments on improved outcomes/need for all GPs to be outfitted with an AED as requiring more study.

REVIEWER	Alexander G. Garza MD, MPH Department of Emergency Medicine Washington Hospital Center Georgetown Univeristy School of Medicine Washington, DC I have no competing interests
REVIEW RETURNED	09-Feb-2013

THE STUDY	Abstract This study is described in the abstract as a prospective cohort study, however this seems to be incorrect. from the manuscript this appears to be either a retrospective case control study or an ongoing data collection for QA purposes. On page 6, introduction, the term AED is misdescribed as "Advisory". AED represents "Automatic External Defibrilator" Page 6 paragraph 3, "overall, a doubling of survival appears to result from early AED use" needs a citation. More than likely, the increase in survival from cardiac arrest is due to improved CPR as well as AED use. Material and Methods The study design was further never mentioned in the "materials and methods section" which is traditionally where you would traditionally find this language. It was described in the abstract as a prospective cohort study, however, if this is a prospective study then a formal study design needs to described including the variables measured and definitive outcomes described. It appears that there were actually 531 practice sites that were enrolled, but data was collected in 495 sites, meaning 36 sites had no data collected (6.7%) which also supports this not being a prospective cohort study. There is no mention of the types of statistical tests that were going to used for various types of data, p values or Confidence Intervals (CI) Page 7, second paragraph. it is unclear what clinical data was

	collected. A study regarding resuscitation outcomes should follow utstien criteria since these are the main predictors of survival from cardiac arrest Page 7, second paragraph, it is undlear what a "mean response rate of 89% actually means. does this mean that 89% of sites provided data or does this mean that of all cases, data was collected on 89% of cases? Page 7, second paragraph "a nurse researcher carried out a semi-structure interview..." has no decription on what is included in the interview
RESULTS & CONCLUSIONS	Results table 1 is confusing because the N changes in the different categories, for instances "shockable rythm" has an n of 263, however the N in ROSC is 272. It is very important to have strict "inclusion criteria" to eliminate bias in the analysis. If key data is unavailable, then the case should be removed from the analysis. Table 4 paragraph, "it is striking that in spite of near equivqalent number of available AED months...urban practices are significantly underrepresented" is incorrect. They are adequately "represented", they are just not utilized as much. this seems entirely logical given that urban areas have much more sophisticated EMS systems that would decrease the opportunity for GP's exposure to CA patients. Page 8, The caluculation of ROSC and survival to discharge was very confusing because the ratios are not described, only the OR. Were these results descriptions of all patient encouters or does this represent the cohort of patients that were treated initially by the GP. It is also interesting to note that the last sentence showed that the OR for the GP AED use first showed no increase in survival, therefore calling into question the utility of GP's attending to CA calls. There is also no historical data to compare survivavl rates pre-study conclusions the conclusion of "good outcomes" having any relationship to GP's attending CA patients is not supported by the evidence

VERSION 1 – AUTHOR RESPONSE

Reviewer: Dr. Richard Verbeek
Assistant Professor, University of Toronto
Toronto, Ontario, Canada

I have no competing interests.

The research question should be better defined. The study is described as reporting the "impact" of

GP use of an AED and advanced life support. Firstly,the only intervention that GPs appear to have provided is the use of an AED. No data on any advanced life has been provided. Secondly, it is unclear if the goal was to measure a) willingness of GPs to respond,b) feasibility of implementing a GP program, c) effect on the GP program in improving a predetermined outcome etc. This appears to be largely a program feasibility study in urban, rural and mixed settings. This should be made clear.

Done. Aim clarified as – 'This study reports incidence and outcomes data for general practitioner (GP) involvement in Cardiac Arrest with Resuscitation Attempt (CARA) in urban, rural and mixed areas of Ireland over a five year period.' Methodology comments below clarify other issues.

It is not clear how sites were selected for participation. Were all 2,000 general practices in Ireland invited initally? Were specific pratices targeted to be invited and if so how were they identified? How many invited practices declined to participate and were these in any way different from those who accepted to participate? It would be useful to more fully describe the practices described as urban, rural, mixed. Perhaps census data about population densities etc is available.

Additional descriptions and clarifications included. We are working with Central Statistics Office data to further refine location and mapping data, for a separate publication.

It would be useful to know something about the training. It may have been reported in the 2009 initial MERIT Project report however it should be summarised here. Was there any follow up training or support for partcipating practices? There is no description as to how the GP "response system" actually functioned. How did a GP even become aware of a cardiac arrest? By what means did a GP respond?

Training described. CARAs originate in participating practices or calls from the community and are not generated by the National Ambulance Service. The absence of any links between NAS and GPs for cardiac arrest alerts is a key issue and is described in the paper. The need to address this is addressed in the discussion.

The main outcome measure is not explictity stated. If the main outcome relates to feasibility then one would want to know how many opportunites there were for GPs to respond and how many opportunities were actually acted on. This data is not reported. It may be that GPs only responsed to a very low proportion of OHCA that they actually were aware of. There may also be substantial differences between urban vs rural vs mixed settings.

Main outcomes are is stated as incidence, ROSC and survival to hospital discharge. We are confident that the data collection method identified a very high proportion of all cardiac arrests in the participating practices. The difference between regions is a central component of results and discussion.

The conclusions and key messages seem to overstate the main findings. They imply that a GP response to an OHCA results in successful outcomes and higher survival rates. The available data do

not support this notion. The conclusions and key messages should focus on the feasibility of implementing this kind of program but should not imply it results in improved outcomes.

Our data indicates that cardiac arrests happen reasonably often in Irish general practice, occur in circumstances where the GP is present before EMS in two-thirds of cases and have up to 19% discharge rates from hospital. We make no claims for special interventions by GPs – however the logic would appear to be that an AED and appropriate training are appropriate for general practices and particularly those in rural areas.

As an observational study to describe the experience of GPs that statisitics are fine. However there is no specific description in the methods regarding calculation of ORs. The ORs are not reported as to whether they are adjusted or unadjusted ORs, although they are likley unadjusted. Clinically it would be important to report an adjusted OR for "GP delivered first AED in relation to hospital discharge" especially if one is attempting to determine whether the GP response is independantly associated with an improved outcome.

These are useful points and the methods section has been improved. The OrRs are unadjusted. The study is not structured or powered to test the hypothesis that GP response is better thant other responses and we are cautious about further interpretation of limited data. However, the hypothesis is a key one and these data may help us to examine it in a further study.

The results support the feasibility of training GPs with the outcome that they respond to OHCA at least some of the time. I think additional information regarding this outcome would be enlightening as previously described. The results do not support the idea that this program leads to increased survival of OHCA.

As above. The survival rate of 19% is clearly higher than other Irish national data reported in the introduction and discussion. However, the GP cardiac arrests are clearly distinct from national OHCA outcomes and we make no claim that GP care per se improves outcome.

I have previously addressed several issues related to interpretation and conclusions. I do not think the data supports the statement in the conclusion that "all GPs in rural practice should be equipped with defibrillators". The data may support it is feasible to do this and that there is a potential for improved outcomes however further light needs to be shed on whether outcomes will actually be improved which to me is a requirement to conclude that all GPs should be equipped. This would ideally be answered by a controlled trial, however given the complexity invovled, a high quality observational study using reqression analysis to determine whether a GP response with an AED to an OHCA is independantly associated with increased survival may be more reasonsable to consider.

As a result the message behind this report is not as clear it could be. Focussing on the feasibility of the MERIT program would go a long way to improving the clarity of the message.

As above.

There is no consort diagram. This could be comprised of how many GP practices there are in Ireland,

how many were invited, how many participated, how many OHCAs there were, how many were responded to by a GP.

These data have been included in the methods section describing the project. Figure 1 summarises recruitment and outcomes.

I find this to be a very intriguing study which describes a highly innovative and potentially promising approach to community response to OHCA. I think this paper would be improved by focussing more clearly on the stucture and feasibility of the MERIT program and limiting comments on improved outcomes/need for all GPs to be outfitted with an AED as requiring more study.

Reviewer: Alexander G. Garza MD, MPH

Department of Emergency Medicine
Washington Hospital Center
Georgetown Univeristy School of Medicine
Washington, DC

I have no competing interests

Abstract
This study is described in the abstract as a prospective cohort study, however this seems to be incorrect.

from the manuscript this appears to be either a retrospective case control study or an ongoing data collection for QA purposes.

Addressed in methods – this is a prospective cohort study which gathered all relevant data from each practice from at the point of recruitment. All cardiac arrests were identified from the time of recruitment specifically for this study.

On page 6, introduction, the term AED is misdescribed as "Advisory". AED represents "Automatic External Defibrilator"

The meaning of the ‘A’ in AED is open to discussion – ‘advisory’ has always been used in our training programmes to emphasise the role of the operator. Technically the descriptor ‘semi-automatic’ has been proposed – but none of these units are automatic defibrillators.

Page 6 paragraph 3, "overall, a doubling of survival appears to result from early AED use" needs a citation. More than likely, the increase in survival from cardiac arrest is due to improved CPR as well as AED use.

Corrected.

Material and Methods

The study design was further never mentioned in the "materials and methods section" which is traditionally where you would traditionally find this language.

It was described in the abstract as a prospective cohort study, however, if this is a prospective study then a formal study design needs to described including the variables measured and definitive outcomes described.

Corrected.

It appears that there were actually 531 practice sites that were enrolled, but data was collected in 495 sites, meaning 36 sites had no data collected (6.7%) which also supports this not being a prospective cohort study.

531 practices have been recruited to date; 495 were recruited during the five year period reported in the paper. Response rates were very high throughout the study period.

There is no mention of the types of statistical tests that were going to used for various types of data, p values or Confidence Intervals (CI)

Corrected.

Page 7, second paragraph. it is unclear what clinical data was collected. A study regarding resuscitation outcomes should follow utstien criteria since these are the main predictors of survival from cardiac arrest

Added.

Page 7, second paragraph, it is undlear what a "mean response rate of 89% actually means. does this mean that 89% of sites provided data or does this mean that of all cases, data was collected on 89% of cases?

Corrected.

Page 7, second paragraph "a nurse researcher carried out a semi-structure interview..." has no decription on what is included in the interview

Added.

Results

table 1 is confusing because the N changes in the different categories, for instances "shockable rythm" has an n of 263, however the N in ROSC is 272. It is very important to have strict "inclusion criteria" to eliminate bias in the analysis. If key data is unavailable, then the case should be removed from the analysis.

Agreed – the method section states that some data is missing, including outcomes for 10 cases. The

denominator changes (and is stated) in some results because these cases have been excluded from the relevant analysis.

Table 4 paragraph, "it is striking that in spite of near equivqalent number of available AED months...urban practices are significantly underrepresented" is incorrect. They are adequately "represented", they are just not utilized as much. this seems entirely logical given that urban areas have much more sophisticated EMS systems that would decrease the opportunity for GP's exposure to CA patients.

Understood.

Page 8, The caluculation of ROSC and survival to discharge was very confusing because the ratios are not described, only the OR. Were these results descriptions of all patient encouters or does this represent the cohort of patients that were treated initially by the GP. It is also interesting to note that the last sentence showed that the OR for the GP AED use first showed no increase in survival, therefore calling into question the utility of GP's attending to CA calls.

Discussed above.

There is also no historical data to compare survivavl rates pre-study

Two relevant Irish data sources are cited, describing national/one region's OHCA outcome data. However, no outcome data from GP cardiac arrests have been available prior to MERIT.

conclusions
the conclusion of "good outcomes" having any relationship to GP's attending CA patients is not supported by the evidence

Discussed at length above. If GPs are providing resuscitation in two-thirds of these case before EMS arrives, it seems reasonable to suggest that there can be benefit.

VERSION 2 – REVIEW

REVIEWER	Verbeek, Rick Sunnybrook Osler Centre for Prehospital Care, Toronto EMS
REVIEW RETURNED	05-Mar-2013

REPORTING & ETHICS	This is a much improved manuscript. The authors have addressed all of my concerns except one. I still do not feel that the statement, "All GPs in rural practice should be equipped with defibrillators." should appear in the conclusion of the body of the manuscript. Firstly, it is at odds with what is stated in the conclusion section of the abstract and with what is described in the strenghts and limitations section. These sections are more appropriately worded. Secondly, the authors showed a non-significant association with "GP AED first on scene" and survival. (Unadjusted OR 1.2 [0.9-1.6 CI]). Given other significant unadjusted OR that were found it is

	likely that the adjusted OR for GP AED will be even lower. Therefore I find their statement puzzling since it is not supported by the evidence. The way I would handle this is to either move it into the discussion where it can be aired more fully as requiring further evaluation or simply delete it from the conclusion along with the following sentence. That way the conclusion as it would remain is compatible with the rest of the manuscript. I recommended this as requiring minor revision but outside of this single "easy to remedy" issue I would recommend acceptance.

REVIEWER	Alexander G. Garza MD, MPH Washington Hospital Center Georgetown University School of Medicine Department of Emergency Medicine Washington, DC
REVIEW RETURNED	10-Mar-2013

THE STUDY	The research question in this study is never clearly defined. The authors state in the abstract that the objective of the study was to "document the involvement of GP's in Cardiac Arrest Resuscitation attempts and describe outcomes". This on its face is a descriptive study, which is appropriate. However, in the following paragraph on Design, the authors state that this is a "five year prospective cohort study". This is not accurate. A cohort study must have a a population that lacks the exposure (presumably treatment by a GP) and a defined outcome (presumaby survival from cardiac arrest). This is not presented in this fashion within the document and does not comport with the "objective" The "intervention" is not what the authors have described, such as training and an AED, rather it is an introduction of ACLS trained GP's into the population.
RESULTS & CONCLUSIONS	Essentially this paper is poorly structured and is unable to answer questions regarding outcomes with any realiability. There is no sorting of the cardiac arrest patients by their encounter with a GP. To analyze the impact to survival that a GP would influence, the subjects included in this study must be sorted by either exposure to a GP or NO exposure to a GP. The data within this study comingle the data making it impossible to draw any conclusions regarding the influence of a GP. It is also difficult to understand if this was a "prospective study" why there was a need for a "modified utstien criteria". These criteria are established so that survival rates can be calculated across different populations. Likewise the statistics involved seem questionable. Univaraiate analysis injects bias into the analysis because of the potential for

	variable interaction. The authors go on to describe what should be a regression analysis instead of univariate analysis The results are not reliable because of no segregation of subjects by exposure to the variable of interest, mainly "exposure to GP" ROSC and discharge statistics are for the entire population and are not specific to the exposure of interest. therefore, it is possible that the survival of patients from cardiac arrest were actually more dependent on the GP's NOT being present. In addition, the denominators in the cardiac arrest analysis are not consistent in Table 1 ranging from 262 to 272. This makes the data unreliable. This practice is repeated in Table 4. As it stands there is no evidence to support the authors conclusions that GP's either enhanced or detracted from the survival of cardiac arrest patients. this paper would need significant reworking including a complete rewrite of the methods and data anyalsis before it could be considered a valid study. The authors would be best served to submit this as a descriptive paper and not try to inject any inferential statistics

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1
This is a much improved manuscript. The authors have addressed all of my concerns except one. I still do not feel that the statement, "All GPs in rural practice should be equipped with defibrillators." should appear in the conclusion of the body of the manuscript. Firstly, it is at odds with what is stated in the conclusion section of the abstract and with what is described in the strenghts and limitations section. These sections are more appropriately worded. Secondly, the authors showed a non-significant association with "GP AED first on scene" and survival. (Unadjusted OR 1.2 [0.9-1.6 CI]). Given other significant unadjusted OR that were found it is likely that the adjusted OR for GP AED will be even lower. Therefore I find their statement puzzling since it is not supported by the evidence. The way I would handle this is to either move it into the discussion where it can be aired more fully as requiring further evaluation or simply delete it from the conclusion along with the following sentence. That way the conclusion as it would remain is compatible with the rest of the manuscript.
I recommended this as requiring minor revision but outside of this single "easy to remedy" issue I would recommend acceptance.

Response: Agreed and implemented.

Reviewer: Alexander G. Garza MD, MPH
Washington Hospital Center
Georgetown University School of Medicine
Department of Emergency Medicine
Washington, DC

The research question in this study is never clearly defined.
The authors state in the abstract that the objective of the study was to "document the involvement of GP's in Cardiac Arrest Resuscitation attempts and describe outcomes". This on its face is a descriptive study, which is appropriate.

However, in the following paragraph on Design, the authors state that this is a "five year prospective cohort study". This is not accurate. A cohort study must have a a population that lacks the exposure (presumably treatment by a GP) and a defined outcome (presumaby survival from cardiac arrest). This is not presented in this fashion within the document and does not comport with the "objective" The "intervention" is not what the authors have described, such as training and an AED, rather it is an introduction of ACLS trained GP's into the population.

Essentially this paper is poorly structured and is unable to answer questions regarding outcomes with any realiability.

There is no sorting of the cardiac arrest patients by their encounter with a GP. To analyze the impact to survival that a GP would influence, the subjects included in this study must be sorted by either exposure to a GP or NO exposure to a GP. The data within this study comingle the data making it impossible to draw any conclusions regarding the influence of a GP.

Response: In the amended version, we make clear that this paper is not structured or powered to compare outcomes of those cardiac arrests treated by a GP with those treated through other response systems in the community. Instead this study prospectively identifies all cardiac arrests managed by GPs and describes the outcomes; no cases are contained in the study other than those managed at some point by a GP. In this case, the cohort under study is the group of GPs participating in MERIT; we report on the proportion ‘exposed’ to cardiac arrest and those ‘not exposed’.

It is also difficult to understand if this was a "prospective study" why there was a need for a "modified utstien criteria". These criteria are established so that survival rates can be calculated across different populations.

Response: The modifications addressed local and general practice issues such as compliance with PHECC CPGs, GPs relationship with the patient involved and grades of EMS practitioners or lay responders involved.

Likewise the statistics involved seem questionable. Univaraiate analysis injects bias into the analysis because of the potential for variable interaction. The authors go on to describe what should be a regression analysis instead of univariate analysis

The results are not reliable because of no segregation of subjects by exposure to the variable of interest, mainly "exposure to GP"

ROSC and discharge statistics are for the entire population and are not specific to the exposure of interest. therefore, it is possible that the survival of patients from cardiac arrest were actually more

dependent on the GP's NOT being present.

Response: The paper sets out to describe incidence and outcomes data and the data reporting framework used is appropriate to that aim, including descriptive statistics and odds ratios for a number of factors. We take a cautious approach to further interpretation of the data, given that this paper is one of the first to propose potential influences on cardiac arrests in general practice and was not structured or powered to test hypotheses or explore causal relationships. Ongoing data collection in this register, informed by the issues identified in this report, will enable the complex relationships between these factors to be addressed in subsequent work.

Response: As described earlier, this paper includes only cardiac arrests managed by GPs and offers no comparison with patients managed by other resources. We cannot therefore comment on the hypothesis that 'the survival of patients from cardiac arrest were actually more dependent on the GP's NOT being present' – however it seems unlikely and would clearly require quite a different study to test.

In addition, the denominators in the cardiac arrest analysis are not consistent in Table 1 ranging from 262 to 272. This makes the data unreliable. This practice is repeated in Table 4.

Response: We clearly state that key data is missing for 10 cases and exclude these cases from some analyses.

As it stands there is no evidence to support the authors conclusions that GP's either enhanced or detracted from the survival of cardiac arrest patients. this paper would need significant reworking including a complete rewrite of the methods and data anyalsis before it could be considered a valid study.

Response: The conclusions have been amended in line with Reviewer 1's comments.

The authors would be best served to submit this as a descriptive paper and not try to inject any inferential statistics